REMARKS

Status of the Claims

Claims 1-3, 5-6, 8-20, 22, 24-29, 31, 33-36, 38, 40-43, 45, 47-50, 52, 54-57, 59, 61-75, 77, 79-86, 88, 90-95, 97, 99-104, 106, 108-113, 115, 117-120 are pending and under examination; Claims 16-20, 22, 24-29, 31, 33-36, 38, 40-43, 45, 47-50, 52, 69-75, 77, 79-86, 88, 90-95, 97, 99-104, 106, 108-113, 115 and 117-120 have been withdrawn.

Applicants respond below to the rejections as they are set forth in the Office Action and respectfully request that the Examiner favorably consider the following remarks.

Restriction Requirement

On September 9, 2009, Applicants' representative elected Group I (Claims 1-3, 5-6, 8-15, 54-57, 59 and 61-68) in a Response to Requirement for Restriction. On December 16, 2009, Applicants' representative further elected the CD45 marker in a Response to Supplemental Restriction Requirement. The Examiner made the restriction final. Consequently, Claims 16-20, 22, 24-29, 31, 33-36, 38, 40-43, 45, 47-50, 52, 69-75, 77, 79-86, 88, 90-95, 97, 99-104, 106, 108-113, 115 and 117-120 are hereby withdrawn from prosecution.

The Rejections Under 35 U.S.C. § 102 Should be Withdrawn

Rejection in view of Fallon et al. (2003) Br. J. Haematol. 122:99-108 or Hess et al. (2003) Blood 102:Abstract No. 383.

Claims 1-3, 5-6, 8-15, 54-57, 59 and 61-68 are rejected under 35 U.S.C. § 102(a) as anticipated by Fallon *et al.* (2003) *Br. J. Haematol.* 122:99-108 or Hess *et al.* (2003) *Blood* 102:Abstract No. 383. The rejection is respectfully traversed.

The claimed invention is directed toward a novel $ALDH^{br}$ stem cell population that has at least 10% CD105 positive cells and that is capable of multilineage development (*i.e.*, comprises hematopoietic stem cells, mesenchymal stem cells and self-renewing progenitor cells; *see*, page 12, lines 5-16, of the above-identified patent application). The population can be isolated, enriched, expanded and/or selected from bone marrow (BM), peripheral blood (PB) or umbilical cord blood (UCB). The claimed invention also is directed toward a novel bone-marrow derived $ALDH^{br}$ stem cell population that likewise is capable of multilineage development.

The Fallon *et al.* reference generally discloses that $ALDH^{br}$ cells can be isolated from PB and that such cells are capable of hematopoietic development (*see*, Summary, Fig. 1, "PBSC SSC^{lo} $ALDH^{br}$ cells enriched in primitive cell with CFU and LTC activity" on pages 103-105, and sentence bridging the first and second columns on page 105).

The Hess *et al.* reference generally discloses that $ALDH^{br}$ cells can be isolated from UCB following lineage depletion (Lin^-) and that such cells are capable of hematopoietic development (lines 17-20). It also discloses that such cells can reconstitute and engraft NOD/SCID mice (lines 20-28). While the Hess *et al.* reference refers to "multilineage development," it is clear that the term is restricted to development of different hematopoietic cell types.

The Fallon *et al.* and Hess *et al.* references are improper citations under § 102 because they do not disclose each and every element as set forth in the pending claims. Specifically, MPEP § 2131 provides:

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) (noting that the identical invention must be shown in as complete detail as is contained in the claims) (emphasis added); *see also*, *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed.Cir. 1989) (noting that the elements must be arranged as required by the claim).

While the Fallon *et al.* and Hess *et al.* references need not satisfy an *ipsissimis verbis* test (*In re Bond*, 910 F.2d 831, 832-833 (Fed. Cir. 1990)), they must disclose the elements "arranged or combined in the same way as in the claim" (*Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1370 (Fed Cir. 2008)).

Here, the claimed $ALDH^{br}$ stem cell population differs from the $ALDH^{br}$ stem cell populations of the Fallon *et al.* and Hess *et al.* references for at least two reasons. First, the claimed $ALDH^{br}$ stem cell population has distinct CD105 expression when compared to the stem cell populations of the Fallon *et al.* and Hess *et al.* references. Applicants submit that the claimed population can be either initially isolated and selected (in the case of BM) or isolated and further selected, enriched and/or expanded (in the case of PB or UCB) to have least 10% CD105 positive cells. As the above-identified patent application clearly discloses, PB does not provide an $ALDH^{br}$ stem cell population having at least 10% CD105 positive cells, as only 1% of

the $ALDH^{br}$ stem cell population from PB expresses CD105 (*see, e.g.*, Table 1 of the above-identified patent application). Therefore, without further selecting, enriching and/or expanding, the $ALDH^{br}$ stem cell population of the Fallon *et al.* reference does not have at least 10% CD105 positive cells as required by the claims.

Likewise, UCB does not provide an $ALDH^{br}$ stem cell population having at least 10% CD105 positive, as less than 1% of the $ALDH^{br}$ stem cell population from UCB expresses CD105 (*see, id.*). Therefore, without further selecting, enriching and/or expanding, the $ALDH^{br}$ stem cell population of the Hess *et al.* reference does not have at least 10% CD105 positive cells as required by the claims.

Second, the claimed $ALDH^{br}$ stem cell population has distinct functional features when compared to the populations of the Fallon *et al.* and Hess *et al.* references. That is, the claimed $ALDH^{br}$ stem cell population is capable of multilineage development (*i.e.*, comprises hematopoietic stem cells, mesenchymal stem cells and self-renewing progenitor cells). In contrast, and as indicated above, the $ALDH^{br}$ stem cell populations of the Fallon *et al.* and Hess *et al.* references are highly enriched in hematopoietic progenitors only. An $ALDH^{br}$ stem cell population expressing CD105, however, has not only hematopoietic stem cell properties, but also mesenchymal stem cell properties. Because the Fallon *et al.* and Hess *et al.* reference do not disclose an $ALDH^{br}$ stem cell population having at least 10% CD105 positive cells, their stem cell populations neither are functionally equivalent to nor inherently possess the features of the claimed $ALDH^{br}$ stem cell population.

Because neither the Fallon *et al.* nor Hess *et al.* references disclose an $ALDH^{br}$ stem cell population having at least 10% CD105 positive cells that is capable of multilineage development, they cannot anticipate the claims. In view of these remarks, Applicants respectfully request that the rejection be withdrawn.

Rejection in view of US Patent No. 5,876,956 by Jones et al. or Int'l Patent Application Publication No. WO 00/34507 by Smith et al.

Claims 1-3, 5-6, 8-15, 54-57, 59 and 61-68 are rejected under 35 U.S.C. § 102(b) as anticipated by US Patent No. 5,876,956 by Jones *et al.* or Int'l Patent Application Publication No. WO 00/34507 by Smith *et al.* The rejection is respectfully traversed.

As noted above, the claimed invention is directed toward a novel $ALDH^{br}$ stem cell population that has at least 10% CD105 positive cells and that is capable of multilineage development (*i.e.*, comprises hematopoietic stem cells, mesenchymal stem cells and self-renewing progenitor cells). The population can be isolated, enriched, expanded and/or selected from BM, PB or UCB. The claimed invention also is directed toward a novel bone-marrow derived $ALDH^{br}$ stem cell population that likewise is capable of multilineage development.

The Jones *et al.* reference generally discloses compositions and methods for isolating $ALDH^{br}$ stem cells with a detectable substrate for aldehyde dehydrogenase such as dansylaminoacetaldehyde (DAAA). Using such compositions and methods, the Jones *et al.* reference discloses human and murine CD34 positive, $ALDH^{br}$ stem cells from BM (Figs. 1A-E and Table 1) that were enriched for hematopoietic progenitors only (third paragraph of Column 9).

Like the Jones *et al.* reference, the Smith *et al.* reference generally discloses compositions and methods for isolating $ALDH^{br}$ stem cells with a detectable substrate for aldehyde dehydrogenase such as BODIPY-aminoacetaldehyde (BAAA) in combination with a multiple drug-resistance (MDR) efflux pump inhibitor. Unlike DAAA, BAAA is alleged to be more suitable for use in isolating human stem cells (*see*, page 2, lines 22-30). Using such compositions and methods, the Smith *et al.* reference discloses an $ALDH^{br}$ stem cell population having at least 50% CD34 positive cells isolated in only a single step from UCB (*see*, page 7, lines 17-22; and page 19, line 18, to page 21, line 3).

The Jones *et al.* and Smith *et al.* references are improper citations under § 102 because they do not disclose each and every element as set forth in the pending claims. *See, e.g.*, *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987); *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed.Cir. 1989); *In re Bond*, 910 F.2d 831, 832-833 (Fed. Cir. 1990); and *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1370 (Fed Cir. 2008); *see also*, MPEP § 2131.

As above, the claimed $ALDH^{br}$ stem cell population differs from the $ALDH^{br}$ stem cell populations of the Jones *et al.* and Smith *et al.* references for at least two reasons. First, the

claimed $ALDH^{br}$ stem cell population has distinct CD105 expression when compared to the stem cell populations of the Jones *et al.* and Smith *et al.* references. With respect to the Jones *et al.* reference, Applicants submit that the claimed $ALDH^{br}$ stem cell population can be isolated from BM by first sorting the $ALDH^{br}$ cells and then assaying for specific cell surface markers such as CD105 (*see*, page 21, line 24, to page 22, line 4, in the above-identified patent application). $ALDH^{br}$ stem cells isolated in this manner have at least 10% CD105 positive cells (*see*, page 22, line 23, to page 23, line 13, of the above-identified patent application). In contrast, the Jones *et al.* reference appears to have isolated its $ALDH^{br}$ stem cell population in the reverse order, thereby resulting in an $ALDH^{br}$ stem cell population that is distinct from the claimed population. That is, the Jones *et al.* reference first sorted BM cells by CD34 expression and then assayed the percentage of $ALDH^{br}$ cells present within the CD34 positive population (*see*, sentence bridging Columns 8-9, as well as FIG. 3, of the Jones *et al.* reference). As the Jones *et al.* reference shows, about 55% of the CD34 positive cells were $ALDH^{br}$ (FIG. 3). Table 2 of the above-identified patent application confirms that about 47 ± 12% of CD34 positive cells are $ALDH^{br}$. However, Table 2 also shows that only 1.34% of such cells are CD105 positive when selected first for CD34. One of skill in the art would be required to further enrich or expand the $ALDH^{br}$ stem cell population of the Jones *et al.* reference, in a manner taught by the above-identified patent application (*see*, *e.g.*, page 4, lines 9-12; page 19, lines 23-29; as well as Examples 5-6, of the above-identified patent application), to arrive at the claimed invention. Therefore, without further selecting, enriching and/or expanding, the $ALDH^{br}$ stem cell population of the Jones *et al.* reference does not have at least 10% CD105 positive cells as required by the claims.

With respect to the Smith *et al.* reference, Applicants note that the claimed $ALDH^{br}$ stem cell population can be isolated and further selected and enriched/expanded from UCB to have least 10% CD105 positive cells. As the above-identified patent application clearly discloses, UCB does not provide an $ALDH^{br}$ stem cell population having at least 10% CD105 positive. In fact, less than 1% of the $ALDH^{br}$ stem cell population from UCB expresses CD105 (*see*, Table 1 of the above-identified patent application). Therefore, without further selecting, enriching and/or expanding, the $ALDH^{br}$ stem cell population of the Smith *et al.* reference does not have at least 10% CD105 positive cells as required by the claims.

Second, the claimed ALDH^{br} stem cell population has distinct functional features when compared to the stem cell populations of the Jones *et al.* and Smith *et al.* references. That is, the claimed ALDH^{br} stem cell population is capable of multilineage development (*i.e.*, comprises hematopoietic stem cells, mesenchymal stem cells and self-renewing progenitor cells). In contrast, and as indicated above, the ALDH^{br} stem cell populations of the Jones *et al.* and Smith *et al.* references are highly enriched in hematopoietic progenitors only. An ALDH^{br} stem cell population expressing CD105, however, has not only hematopoietic stem cell properties, but also mesenchymal stem cell properties. Because the Jones *et al.* and Smith *et al.* references do not disclose an ALDH^{br} stem cell population having at least 10% CD105 positive cells, their stem cell populations neither are functionally equivalent to nor inherently possess the features of the claimed ALDH^{br} stem cell population.

Because neither the Jones *et al.* nor Smith *et al.* reference discloses an ALDH^{br} stem cell population having at least 10% CD105 positive cells that is capable of multilineage development, they cannot anticipate the claims. In view of these remarks, Applicants respectfully request that the rejection be withdrawn.

Conclusion and Fees

In view of the aforementioned amendments and remarks, Applicants respectfully submit that the novelty issues are overcome. Accordingly, Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 C.F.R. § 1.136(a), and any fee

required therefor (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

/w. murray spruill/

W. Murray Spruill
Registration No. 32,943

Customer No. 00826
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel Raleigh Office: (919) 862-2200
Fax Raleigh Office: (919) 862-2260

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